Claims

1. A method of treating hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors, in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

2. A method of treating hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors, in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof in combination with an effective amount of an HMG Co-A reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

3. A pharmaceutical composition which comprises an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, in association with a pharmaceutically acceptable diluent or carrier for use in the treatment of hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors.

4. A pharmaceutical composition which comprises an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, in association with a pharmaceutically acceptable diluent or carrier, in combination with a pharmaceutical composition which comprises an HMG Co-A reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, in association with a pharmaceutically acceptable diluent or carrier for use in the treatment of hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors.

5. A pharmaceutical composition which comprises an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, and an HMG Co-A reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, in association with a pharmaceutically acceptable diluent or carrier for use in the treatment of hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors.

6. The use of an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, in the manufacture of a medicament for use in the treatment of hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors, in a warm-blooded animal, such as man.

7. The use of an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, in combination with an HMG Co-A reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, in the manufacture of a medicament for use in the treatment of hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors, in a warm-blooded animal, such as man.

8. The use of an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, in the treatment of hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors, in a warm-blooded animal, such as man.

9. The use of an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, in combination with an HMG Co-A reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, in the treatment of hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors, in a warm-blooded animal, such as man.

10. A method of testing whether an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof has any one of the following effects:
i) lowering total cholesterol; optionally in combination with an HMG CoA reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;
ii) lowering LP-remnants; optionally in combination with an HMG CoA reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;
iii) lowering LDL; optionally in combination with an HMG CoA reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;
iv) raising HDL; optionally in combination with an HMG CoA reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof; or
v) exhibits a synergistic effect in combination with an HMG CoA reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof on the lowering of the ratio of (LP-remnants + LDL-cholesterol)/(HDL-cholesterol);
wherein the method of testing comprises administering the IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, to a transgenic LDL receptor and/or ApoE deficient non-human mammal optionally in combination with an HMG CoA reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof; and determining whether there has been an effect on any one of (i) - (v) above on the non human mammal.

11. A combination comprising an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, and an HMG Co-A reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, for use in the treatment of hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors.

12. A combination comprising an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, and an HMG Co-A reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, for use in lowering abnormal cholesterol and triglyceride levels and the composition of the different lipoproteins concerning cholesterol, triglycerides, and apolipoproteins in a warm-blooded

animal, such as man, with hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors.

13. The method of treatment, pharmaceutical composition, use, method of testing or combination according to any one of claims 1-12 wherein the IBAT inhibitor is (3*R*,5*R*)-3-butyl-3-ethyl-1,1-dioxido-5-phenyl-2,3,4,5-tetrahydro-1,4-benzothiazepin-8-yl β-D-glucopyranosiduronic acid or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

14. The method of treatment, pharmaceutical composition, use, method of testing or combination according to any one of claims 1-12 wherein the IBAT inhibitor is selected from:
1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)-1'-phenyl-1'-[*N'*-(carboxymethyl) carbamoyl]methyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)-α-[*N'*-(carboxymethyl)carbamoyl]-4-hydroxybenzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)-1'-phenyl-1'-[*N'*-(2-sulphoethyl)carbamoyl]methyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(*N*-{(R)-1'-phenyl-1'-[*N'*-(2-sulphoethyl)carbamoyl]methyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)-α-[*N'*-(2-sulphoethyl)carbamoyl]-4-hydroxybenzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(*N*-{(R)-α-[*N'*-(2-sulphoethyl) carbamoyl]-4-hydroxybenzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(*N*-{(R)-α-[*N'*-(2-carboxyethyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)-α-[*N'*-(2-carboxyethyl)carbamoyl]-4-hydroxybenzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(*N*-{(R)-α-[*N'*-(5-carboxypentyl) carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)-α-[*N'*-(2-carboxyethyl)carbamoyl] benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;

1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{α-[*N'*-(2-sulphoethyl)carbamoyl]-2-fluorobenzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;

1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(*N*-{(R)-α-[*N'*-(R)-(2-hydroxy-1-carboxyethyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;

1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)-α-[*N'*-(R)-(2-hydroxy-1-carboxyethyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;

1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-{*N*-[(R)-α-(*N'*-{(R)-1-[*N''*-(R)-(2-hydroxy-1-carboxyethyl)carbamoyl]-2-hydroxyethyl}carbamoyl)benzyl]carbamoylmethoxy}-2,3,4,5-tetrahydro-1,5-benzothiazepine;

1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(*N*-{α-[*N'*-(carboxymethyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;

1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(*N*-{α-[*N'*-((ethoxy)(methyl)phosphoryl-methyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;

1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-{*N*-[(R)-α-(*N'*-{2-[(hydroxy)(methyl)phosphoryl]ethyl}carbamoyl)benzyl]carbamoylmethoxy}-2,3,4,5-tetrahydro-1,5-benzothiazepine;

1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)-α-[*N'*-(2-methylthio-1-carboxyethyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;

1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-{*N*-[(R)-α-(*N'*-{2-[(methyl)(ethyl) phosphoryl]ethyl}carbamoyl)-4-hydroxybenzyl]carbamoylmethoxy}-2,3,4,5-tetrahydro-1,5-benzothiazepine;

1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-{*N*-[(R)-α-(*N'*-{2-[(methyl)(hydroxy) phosphoryl]ethyl}carbamoyl)-4-hydroxybenzyl]carbamoylmethoxy}-2,3,4,5-tetrahydro-1,5-benzothiazepine;

1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)-α-[(R)-*N'*-(2-methylsulphinyl-1-carboxyethyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine; and

1,1-dioxo-3,3-dibutyl-5-phenyl-7-methoxy-8-[*N*-{(R)-α-[*N'*-(2-sulphoethyl)carbamoyl]-4-hydroxybenzyl}carbamoylmethoxy]-2,3,4,5-tetrahydro-1,5-benzothiazepine;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

15. The method of treatment, pharmaceutical composition, use, method of testing or combination according to any one of claims 2, 4, 5, 7, 9, 10, 11, 12, 13 or 14 wherein the HMG CoA reductase inhibitor is selected from fluvastatin, lovastatin, pravastatin, simvastatin, atorvastatin, cerivastatin, bervastatin, dalvastatin, mevastatin and rosuvastatin, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

16. The method of treatment, pharmaceutical composition, use, method of testing or combination according to any one of claims 2, 4, 5, 7, 9, 10, 11, 12, 13, 14 or 15 wherein the HMG CoA reductase inhibitor is atorvastatin calcium salt.

17. The method of treatment, pharmaceutical composition, use, method of testing or combination according to any one of claims 2, 4, 5, 7, 9, 10, 11, 12, 13, 14 or 15 wherein the HMG CoA reductase inhibitor is rosuvastatin calcium salt.

18. The method of treatment, pharmaceutical composition, use, method of testing or combination according to any one of claims 1-17 wherein "hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors" is the disease state familial hypercholesterolemia.

19. The method of treatment, pharmaceutical composition, use, method of testing or combination according to any one of claims 1-17 wherein "hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors" is the disease state familial defective apolipoprotein B 100.

20. The method of treatment, pharmaceutical composition, use, method of testing or combination according to any one of claims 1-17 wherein "hypercholesterolemia and/or other forms of dyslipidaemia wherein said hypercholesterolemia and dyslipidaemias are characterized by defects in lipoproteins or their receptors" is the disease state type III dyslipidaemia.